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GLOBAL STABILITY OF VIRUS PERSISTENCE OF A MATHEMATICAL MODEL OF THE DYNAMICS OF EBOLA VIRUS INFECTION IN HUMAN CELL POPULATION

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Abstract

In this paper, we formulated a mathematical model of the dynamics of Ebola virus infection in human cell population, using ordinary differential equation. We have shown the positivity of solutions of the model equations. The virus free and virus persistence equilibrium points were obtained. We computed the basic reproduction number of the system and shown the global stability of virus persistence equilibrium state.

Keywords: Mathematical model; Ebola virus; Immune response; Positivity; Global stability

1.0 Introduction

Ebola virus is a long filamentous, enveloped virus, consisting of a negative sense single-structural Ribonucleic acid (ssRNA) virus, un-segmented and the genome of the Ebola virus is encoded with Seven structural proteins and two non-structural proteins, such as, Glycoprotein (GP); Nucleoprotein (NP); viral protein 24 (VP24); viral protein 30 (VP30); viral protein 35 (VP35); viral protein 40 (VP40); and RNA-polymerase protein (L-polymerase) [1,2]. Ebola virus belongs to a family of filoviridae [2]. The virus is classified in to five distinct species namely, Reston Ebola virus; Cotes d'Ivoire Ebola virus; Bundibugyo Ebola virus; Sudan Ebola virus; and Zaire Ebola virus [2].

The virus was first discovered in 1976 in Democratic Republic of Congo [3]. Recently, the virus again resurfaced in some West Africa Countries like Guinea, Sierra Leone, Liberia and Nigeria. The latest eruption of the virus was the deadliest in its history [4]. There was an outbreak of the virus between December 2013 and 2015, which was referred to as Zaire Ebola species and known as Ebola virus [2]. It causes serious incidence of haemorrhagic fever and illness in humans who are exposed to the virus [5]. It was reported that at least a total of 23,014 cases occurred of which 9, 840 resulted to deaths [6]. In Nigeria, it was confirmed that a total of 19 cases occurred, of which seven (7) died and twelve (12) survived a fatality rate of 40% compared to 70% fatality rate reported in other Africa Countries [7].

The incubation period of Ebola virus ranges from 2 to 21 days and infectious periods ranges from 4 to 10 days [8]. Meanwhile, it takes an approximation of 31 days to quarantine a patient under investigation of the Ebola virus. Consequently, the symptoms of the Ebola virus are characterized by headaches, fever, vomiting, bleeding diarrhea, and rash [9] in infected person, severe bleeding and shock are usually followed by death. The World Health Organisation has not yet approved any vaccine or antiviral drugs for Ebola virus, rather a trial vaccine is been administer on patients [2]. The spread of the virus and eventual death of infected patients was largely contained (reduced) through early detection and effective contact tracing [1].

Ebola virus is known to cause damage to large variety of cell types including monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes, and several types of epithelial cells. The primary targets of the virus are dendritic, monocytes and macrophage cells. These are the cells infected in the early stage of the virus infection in the body which spread through the organs [10].

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Macrophage encounter APC and release a protein called interlenkin-1(IL-1) that acts as a chemical alarm signal; Helper T-cells respond to interlekin-1 and release interlenkin-2(IL-2) by simultaneously initiating two parallel lines of immune system defence: the cell-mediated response carried out by T-cells, and humoral response carried out by B-cells [11]. The organization of this paper is as follows, in the next section, we present the formation of our model equations, we establish virus free equilibrium state and virus persistence equilibrium and we obtain the basic reproduction number of the infection and determined the global stability of the virus persistence equilibrium state.

2.0 MATERIAL AND METHOD

Model Formulation

The model equations are formulated using ordinary differential equation. A mathematical model of the dynamics of Ebola virus infection in the cell population and immune response is developed by incorporating humoral immunity, vaccination and clearance of the free virus. The cell population is partitioned into five compartments, these are: U(t) = the Uninfected cells, this is the class in which cell population are free from the virus but open to infection as they interact with the free virus class; I(t) = Infected cells, this the class in which the cell is infected and are infectious; V(t) = free Virus class, this is the class that interact with healthy cells to become infected; T(t) = Cytotoxic T-Lymphocyte (CTL), this is the class that kill infected cell from the cell population; B(t) = Humoral immunity produce by B-cells, this is the class that clear the free virus from the system.

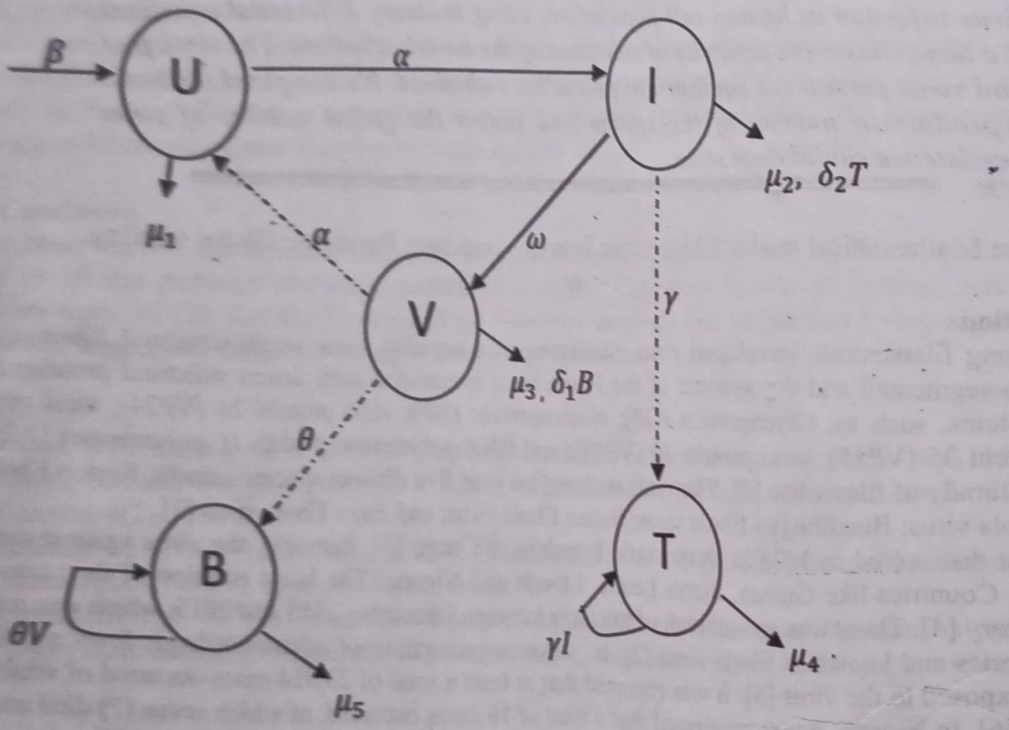

Figure 1: Schematic representation for the model

$$\frac{dU}{dt} = \beta - \mu_1 U - \alpha U.V \quad (1)$$

$$\frac{dI}{dt} = \alpha U.V - \mu_2 I - \delta_1 I.T \quad (2)$$

$$\frac{dV}{dt} = \omega I - \mu_3 V - \delta_2 B.V \quad (3)$$

$$\frac{dT}{dt} = \gamma I.T - \mu_4 T \quad (4)$$

$$\frac{dB}{dt} = \theta B.V - \mu_5 B \quad (5)$$

Table 1: Parameters of the Model

Symbols	Description
β	Reproduction rate of uninfected cell
α	Infection rate of uninfected cell
ω	Reproduction rate of Virus
γ	Reproduction rate of Cytotoxic T-cells in response to infected cell
θ	Reproduction rate of antibodies in response to Ebola virus exposure
δ_1	Clearance rate of infected cells by Cytotoxic T-cell response
δ_2	Clearance rate of the viruses by antibodies
μ_1	Natural death rate of uninfected cell
μ_2	Death rate of infected cell
μ_3	Death/Decay rate of the virus
μ_4	Death/Decay rate of Cytotoxic T-cell
μ_5	Death/Decay rate of B-cell secreted antibodies

RESULTS AND DISCUSSION

POSITIVITY OF SOLUTIONS OF THE MODEL EQUATIONS

In this section, we to prove that all the solutions to the system of ODEs are positive for all time $t > 0$.

Theorem 1: All the solutions of the model equations (1)- (5) are positive for all time $t > 0$ provided that the initial conditions are positive, that is, $U(0) > 0, I(0) > 0, V(0) > 0, T(0) > 0, B(0) > 0$. Then, the solution set $U(t), I(t), V(t), T(t), B(t)$ will be positive in $\mathbb{R}^5_+$

Proof: Assuming that all the parameters are nonnegative, from (1), we have

$$\frac{dU}{dt} = \beta - \mu_1 - \alpha U.V \quad (6)$$

$$\geq -\mu_1 U - \alpha U.V \quad (7)$$

Integrating (7) gives

$$\int \frac{dU}{U} = -\int (\mu_1 + \alpha V) dt$$

$$U(t) \geq U(0) e^{-\mu_1 t - \alpha \int V(t) dt}$$

$$U(t) \geq 0$$

Similarly, we have $I(t) \geq 0, V(t) \geq 0, T(t) \geq 0, B(t) \geq 0$ (8)

Thus, for all $t \in [0, \infty)$, $U(t), I(t), V(t), T(t), B(t)$ will be positive and remain in $\mathbb{R}^5_+$

EXISTENCE OF EQUILIBRIUM STATE, (E^*)

Equilibrium States of the Model

At equilibrium states, $\frac{dU}{dt} = \frac{dI}{dt} = \frac{dV}{dt} = \frac{dT}{dt} = \frac{dB}{dt} = 0$ (9)

Let $(U, I, V, T, B) = (U^*, I^*, V^*, T^*, B^*)$

We have the following

$$\beta - \mu_1 U^* - \alpha U^*.V^* = 0 \quad (10)$$

$$\alpha U^*.V^* - \mu_2 I^* - \delta_1 I^*.T^* = 0 \quad (11)$$

$$\omega I^* - \mu_3 V^* - \delta_2 B^*.V^* = 0 \quad (12)$$

$$\gamma I^*.T^* - \mu_4 T^* = 0 \quad (13)$$

$$\theta B^*.V^* - \mu_5 B^* = 0 \quad (14)$$

From (12), we have

$$V^* = \frac{\omega I^*}{\mu_3 + \delta_2 B^*} \quad (15)$$

Substitute V^* in (5) into (11), we have

$$\alpha U^*.\left(\frac{\omega I^*}{\mu_3 + \delta_2 B^*}\right) - \mu_2 I^* - \delta_1 I^*.T^* = 0$$

Implies

$$I^*\{\alpha U^* \frac{\omega}{\mu_3 + \delta_2 B^*} - \mu_2 - \delta_1 T^*\} = 0 \quad (16)$$

From (16) we have

$$I^* = 0$$

And $\frac{\alpha\omega U^*}{\mu_3+\delta_2 B^*} - \mu_2 - \delta_1 T^* = 0$ (17)

From (13), we have

$T^*(\gamma I^* - \mu_4) = 0$

Implies, $T^* = 0$

Or $I^* = \frac{\mu_4}{\gamma}$ (18)

From (14), we have

$B^*(\theta . V^* - \mu_5) = 0$

Implies, $B^* = 0$

Or $V^* = \frac{\mu_5}{\theta.}$ (19)

Substitute I^* in (17), T^* in (18) and B^* in (19) into (15), we have

$V^* = 0$ (20)

Substitute I^* in (17) and V^* in (20) into (10), we have

$U^* = \frac{\beta}{\mu_1}$ (21)

Therefore, the virus free equilibrium is given as,

$(U^*, I^*, V^*, T^* B^*) = (U^0, I^0, V^0, T^0 B^0) = \left(\frac{\beta}{\mu_1}, 0, 0, 0, 0\right)$ (22)

Substitute $V^* = \frac{\mu_5}{\theta.}$ in (19) into (10), we have

$\beta - \mu_1 U^* - \alpha U^*(\frac{\mu_5}{\theta}) = 0$

Implies $U^* = \frac{\beta\theta}{\theta\mu_1+\alpha\mu_5}$ (23)

Substitute I^* in (18), V^* in (19) and U^* in (23) into (11), we have

$\alpha.\frac{\beta\theta}{\theta\mu_1+\alpha\mu_5}.\frac{\mu_5}{\theta} - \mu_2.\frac{\mu_4}{\gamma} - \delta_1\frac{\mu_4}{\gamma}.T^* = 0$ (24)

Simplification of the above gives

$\frac{\alpha\beta\mu_5}{\theta\mu_1+\alpha\mu_5} - \frac{\mu_2\mu_4}{\gamma} - \frac{\delta_1\mu_4}{\gamma}.T^* = 0$

Implies,

$T^* = \frac{\gamma(\alpha\beta\mu_5\gamma - \mu_2\mu_4(\theta\mu_1+\alpha\mu_5)}{\gamma\delta_1\mu_4(\theta\mu_1+\alpha\mu_5)}$

Therefore, we have

$T^* = \frac{(\alpha\beta\mu_5\gamma - \mu_2\mu_4(\theta\mu_1+\alpha\mu_5)}{\delta_1\mu_4(\theta\mu_1+\alpha\mu_5)}$ (25)

Substitute $I^* = \frac{\mu_4}{\gamma}$ in (18) and $V^* = \frac{\mu_5}{\theta.}$ in (19) into (12), we have

$\omega\left(\frac{\mu_4}{\gamma}\right) - \mu_3\left(\frac{\mu_5}{\theta.}\right) - \delta_2 B^*.(\frac{\mu_5}{\theta}) = 0$

$\frac{\omega\mu_4}{\gamma} - \frac{\mu_3\mu_5}{\theta} - \frac{\delta_2 B^*\mu_5}{\theta} = 0$ (26)

From (26), we have

$B^* = \frac{\omega\mu_4\theta - \mu_3\mu_5\gamma}{\delta_2\mu_5\gamma}$ (27)

Therefore, the Virus Persistence Equilibrium (VPE) is given as,

$(U^*, I^*, V^*, T^* B^*) = (U^{**}, I^{**}, V^{**}, T^{**} B^{**})$

$= (\frac{\beta\theta}{\theta\mu_1+\alpha\mu_5}, \frac{\mu_4}{\gamma}, \frac{\mu_5}{\theta.}, \frac{(\alpha\beta\mu_5\gamma - \mu_2\mu_4(\theta\mu_1+\alpha\mu_5)}{\delta_1\mu_4(\theta\mu_1+\alpha\mu_5)}, \frac{\omega\mu_4\theta - \mu_3\mu_5\gamma}{\delta_2\mu_5\gamma})$ (28)

COMPUTATION OF BASIC REPRODUCTION NUMBER, R_0

The Basic Reproduction number denoted by R_0 is the average number of secondary cases generated by a virus w introduced into a cell population. To control the virus population, it is required that $R_0 < 1$ [12]. In this case, infected cell produces on average less than one newly infected case over the course of its infection period. In this ca the virus will be eliminated from the system and individual will recover from the infection. On the other hand, if R_0 1 then the infected individual cells produces on average more than one new infected case and the infection will pers in the cells population.

We applying next generation matrix operator to compute the basic reproduction number [13]. The basic reproducti number is obtained by dividing the whole population into n compartments in which there are m infected compartme m < n. Let x_i, $i = 1,2,3,\ldots,m$ be the number of infected individual in the i^{th} compartment at time t.

The largest Eigenvalue or spectral radius of FV^{-1} is the basic reproduction number of the model

$$FV^{-1} = \left[\frac{\partial F_i(E^0)}{\partial x_j}\right]\left[\frac{\partial V_i(E^0)}{\partial x_j}\right]^{-1}$$

Where F_i is the rate of appearance of new infection in compartment i, V_i is the transfer of infection from one compartment i to another and $E^0$is the Disease-Free Equilibrium. Using this technique, we have spectral radius (ρ) of the next generation matrix, FV^{-1} that is, $R_0 = \rho(FV^{-1})$. Therefore, we have

$$f = \begin{pmatrix} f_1 \\ f_2 \end{pmatrix} = \begin{pmatrix} \omega I \\ \alpha UV \end{pmatrix} \tag{29}$$

Differentiate (29) partially with respect to time gives

$$F = \begin{pmatrix} \frac{\partial f_1}{\partial V} & \frac{\partial f_1}{\partial I} \\ \frac{\partial f_2}{\partial V} & \frac{\partial f_2}{\partial I} \end{pmatrix} = \begin{pmatrix} 0 & \omega \\ \alpha U & 0 \end{pmatrix} \tag{30}$$

At virus-free equilibrium (VFE)

$$F = \begin{pmatrix} 0 & \omega \\ \frac{\alpha\beta}{\mu_1} & 0 \end{pmatrix} \tag{31}$$

Given that,

$$v = \begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = \begin{pmatrix} (\mu_3 + \delta_2 B)V \\ (\mu_2 + \delta_1 T)I \end{pmatrix} \tag{32}$$

Differentiate (32) partially with respect to time, we have,

$$V = \begin{pmatrix} \frac{\partial v_1}{\partial V} & \frac{\partial v_1}{\partial I} \\ \frac{\partial v_2}{\partial V} & \frac{\partial v_2}{\partial I} \end{pmatrix}$$

Implies,

$$V = \begin{pmatrix} (\mu_3 + \delta_2 B^0) & 0 \\ 0 & (\mu_2 + \delta_1 T^0) \end{pmatrix} \tag{33}$$

Let

$$k_1 = (\mu_3 + \delta_2 B^0)$$
$$k_2 = (\mu_2 + \delta_1 T^0) \tag{34}$$

We have,

$$V^{-1} = \frac{adjV}{\det V} \tag{35}$$

Implies,

$$V^{-1} = \frac{adjV}{\det V} = \frac{1}{k_1 k_2}\begin{pmatrix} k_2 & 0 \\ 0 & k_1 \end{pmatrix}$$

$$V^{-1} = \frac{1}{k_1 k_2}\begin{pmatrix} k_2 & 0 \\ 0 & k_1 \end{pmatrix} \tag{36}$$

Multiplying (31) and (36) gives

$$FV^{-1} = \frac{1}{k_1 k_2}\begin{pmatrix} 0 & \omega \\ \frac{\alpha\beta}{\mu_1} & 0 \end{pmatrix}\begin{pmatrix} k_2 & 0 \\ 0 & k_1 \end{pmatrix} \tag{37}$$

Solving (37), we have

$$FV^{-1} = \frac{1}{k_1 k_2}\begin{pmatrix} 0+0 & \omega k_1 \\ \frac{\alpha\beta k_2}{\mu_1} - 0 & 0+0 \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\omega k_1}{k_1 k_2} \\ \frac{\alpha\beta k_2}{k_1 k_2 \mu_1} & 0 \end{pmatrix}$$

Implies,

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\omega}{k_2} \\ \frac{\alpha\beta}{k_1\mu_1} & 0 \end{pmatrix} \tag{38}$$

The characteristics equation of (38) gives

$$\begin{vmatrix} -\lambda & \frac{\alpha}{k_2} \\ \frac{\alpha\beta}{k_2\mu_1} & -\lambda \end{vmatrix} = 0 \quad (39)$$

$$\lambda^2 - \left(\frac{\alpha}{k_2}\cdot\frac{\alpha\beta}{k_2\mu_1}\right) = 0$$

$$\lambda^2 = \left(\frac{\alpha}{k_2}\cdot\frac{\alpha\beta}{k_2\mu_1}\right) = \frac{\alpha\omega\beta}{k_2^2\mu_1}$$

Implies,

$$\lambda^2 = \frac{\alpha\omega\beta}{(\mu_1+\delta_2 T^{**})(\mu_2+\delta_2 B^{**})\mu_1}$$

$$\lambda = \sqrt{\frac{\alpha\omega\beta}{(\mu_1+\delta_2 T^{**})(\mu_2+\delta_2 B^{**})\mu_1}} \quad (40)$$

λ is the spectral radius of $\rho(FV^{-1})$

$$R_0 = \sqrt{\frac{\alpha\omega\beta}{(\mu_1+\delta_2 T^{**})(\mu_2+\delta_2 B^{**})\mu_1}} \quad (41)$$

The equation (41) is the basic reproduction number of infected cell of system (1)-(5).

GLOBAL STABILITY OF VIRUS PERSISTENCE EQUILIBRIUM STATE (E^{**})

Lyapunov function of the Goh-Voltera type which is nonlinear is used for proving of the Global asymptotic stability of the Endemic Equilibrium Point (EEP) which is known as Virus Persistence and Immunes Persistence Equilibrium State, (VIEP)

Theorem 2: The unique virus and immunes persistence equilibrium of the model (1)-(5), is globally asymptotically stable (GAS) if $R_0 > 1$ & $R_1 > 1$

Proof:

Consider the model (1)-(5), let $R_0 > 1$. Consider the following non-linear Lyapunov function for the sub-system model involving the state variables, U, V, and I. Let

$$F = U - U^{**} - U^{**}\ln\left(\frac{U}{U^{**}}\right) + V - V^{**} - V^{**}\ln\left(\frac{V}{V^{**}}\right) + A\left(I - I^{**} - I^{**}\ln\left(\frac{I}{I^{**}}\right)\right) \quad (42)$$

The Lyapunov derivative from equation (42), $\dot{F}$, gives

$$\dot{F} = \left(\dot{U} - \frac{U^{**}}{U}\dot{U}\right) + \left(\dot{V} - \frac{V^{**}}{V}\dot{V}\right) + A\left(\dot{I} - \frac{I^{**}}{I}\dot{I}\right) \quad (43)$$

Substitute the right hand equations in the model (1)-(3) into the expression in (43), we have

$$\dot{F} = \beta - \mu_1 U - \alpha U.V - \frac{U^{**}}{U}(\beta - \mu_1 U - \alpha U.V)$$

$$+\omega I - \mu_2 V - \delta_2 B.V - \frac{V^{**}}{V}(\omega I - \mu_2 V - \delta_2 B.V)$$

$$+A(\alpha U.V - \mu_2 I - \delta_2 I.T - \frac{I^{**}}{I}(\alpha U.V - \mu_2 I - \delta_2 I.T)) \quad (44)$$

Simplification of (44) gives,

$$\dot{F} = \beta - \mu_1 U - \alpha U.V - \frac{U^{**}\beta}{U} + \mu_1 U^{**} + \alpha U^{**}.V$$

$$+\omega I - \mu_2 V - \delta_2 B.V - \frac{V^{**}}{V}\omega I + \mu_2 V^{**} + \delta_2 B.V^{**}$$

$$+A(\alpha U.V - \mu_2 I - \delta_2 I.T - \frac{I^{**}}{I}\alpha U.V + \mu_2 I^{**} + \delta_2 I^{**}.T) \quad (45)$$

Substitute the equation (6) of the model into equation (45)

$$\dot{F} = \beta - \mu_1 U - \alpha U.V - \frac{U^{**}\beta}{U} + \mu_1 U^{**} + \alpha U^{**}.V$$

$$+\omega I - \mu_2 V - \delta_2 B.V - \frac{V^{**}}{V}\omega I + \mu_2 V^{**} + \delta_2 B.V^{**}$$

$$+\alpha AU.V - \mu_2 AI - \delta_2 AI.T - \frac{I^{**}}{I}\alpha AU.V + \mu_2 AI^{**} + \delta_2 AI^{**}.T \quad (46)$$

At endemic steady state, we note that from equation (1)-(5), we have the following relation

$$\beta = \mu_1 U^{**} + \alpha U^{**}V^{**} \quad (47)$$

$$\omega I^{**} = \mu_2 V^{**} + \delta_2 B^{**}.V^{**} \quad (48)$$

$$\alpha U^{**}.V^{**} = \mu_2 I^{**} + \delta_2 I^{**}.T^{**} \quad (49)$$

$$\gamma I^{**}.T^{**} = \mu_4 T^{**} \quad (50)$$

$$\theta B^{**}.V^{**} = \mu_3 B^{**} \quad (51)$$

substitute the expression of β in equation (47) into the equation (46)

$$\dot{F} = \mu_1 U^{**} + \alpha U^{**} V^{**} - \mu_1 U - \alpha U^{**} V - \frac{U^{**}(\mu_1 U^{**} + \alpha U^{**} V^{**})}{U} + \mu_1 U^{**} + \alpha U^{**} V$$

$$+\omega I - \mu_3 V - \delta_2 \beta^{**} V = \frac{I^{**}}{V}\omega I + \mu_3 V^{**} + \delta_2 \beta^{**} V^{**}$$

$$+\alpha A U^{**} V - \mu_2 A I - \delta_1 A I^{**} T = \frac{I^{**}}{V}\alpha A U^{**} V + \mu_2 A I^{**} + \delta_1 A I^{**} T \quad (52)$$

We select the terms, where the infected classes are without the three stars on them, (i.e V, I) these terms are now collected together, we have

$$-\alpha U^{**} V + \alpha U^{**} V + \omega I - \mu_3 V - \delta_2 \beta^{**} V + \alpha A U^{**} V - \mu_2 A I - \delta_1 A I^{**} T \quad (53)$$

We equate equation (53) to zero (0), and find the value of A, now to determine A, collecting the terms in infected (I) only, or the coefficients of the infected term from equation (53), we have

$$\omega I - \mu_2 A I - \delta_1 A I^{**} T = 0 \quad (53)$$

implies,

$$\omega I - A(\mu_2 + \delta_1 T^{**})I = 0 \quad (54)$$

Making A subject of formula, we have,

$$A = \frac{\omega}{(\mu_2 + \delta_1 T^{**})} \quad (55)$$

To confirm that the expression in (53) is zero (0), we have

$$-(\alpha U^{**})V + \alpha U^{**}(V) + \omega I - \mu_3 V - \delta_2 \beta^{**} V + (\alpha U)A^{**} V + (-\mu_2 I - \delta_1 I^{**} T)A = 0 \quad (56)$$

implies,

$$-\left(\frac{\mu_2 + \delta_1 T^{**}}{V}\right)V + \alpha U^{**}\left(\frac{\mu_2 + \delta_1 T^{**}}{\alpha U^{**}}\right)I + \omega I - \omega I + \left(\frac{\mu_2 + \delta_1 T^{**}}{V}\right)I\left(\frac{\omega}{(\mu_2 + \delta_1 T^{**})}\right)V$$

$$-(\mu_2 I + \delta_1 I^{**} T)\left(\frac{\omega}{(\mu_2 + \delta_1 T^{**})}\right) = 0 \quad (57)$$

Reduced to

$$-(\mu_2 + \delta_1 T^{**})I + (\mu_2 + \delta_1 T^{**})I + \omega I - \omega I + (I)(\omega) - (I)(\omega) = 0 \quad (58)$$

Since (53) is equal to zero (0), the expression of $\dot{F}$ in (52), reduced to the following,

$$\dot{F} = \mu_1 U^{**} + \alpha U^{**} V^{**} - \mu_1 U - \frac{\mu_1 U^{**2}}{U} - \frac{\alpha U^{**2} V^{**}}{U} + \mu_1 U^{**}$$

$$-\frac{V^{**}}{V}\omega I + \mu_3 V^{**} + \delta_2 \beta^{**} V^{**} - \frac{I^{**}}{I}\alpha\left(\frac{\omega}{(\mu_2 + \delta_1 T^{**})}\right)U^{**} V$$

$$+\mu_2\left(\frac{\omega}{(\mu_2 + \delta_1 T^{**})}\right)I^{**} + \delta_1\left(\frac{\omega}{(\mu_2 + \delta_1 T^{**})}\right)I^{**} T \quad (59)$$

Since $\frac{I}{\mu_2 + \delta_1 T} = \frac{I^{**}}{\alpha U^{**} V^{**}}$ and $\frac{\omega}{(\mu_3 + \delta_2 \beta)} = \frac{V^{**}}{I^{**}}$ at steady state from equation (2) and (3), then we substitute into equation (59), we have,

$$\dot{F} = \mu_1 U^{**}\left(2 - \frac{U}{U^{**}} - \frac{U^{**}}{U}\right) + \alpha U^{**} V^{**} - \frac{\alpha U^{**2} V^{**}}{U} - \frac{V^{**}}{V}\omega I + \omega I^{**}$$

$$-\frac{I^{**}}{I}\alpha\left(\frac{I^{**}\omega}{\alpha U^{**} V^{**}}\right)U^{**} V + \mu_2\left(\frac{I^{**}\omega}{\alpha U^{**} V^{**}}\right)I^{**} + \delta_1\left(\frac{\omega I^{**}}{\alpha U^{**} V^{**}}\right)I^{**} T \quad (60)$$

implies,

$$\dot{F} = \mu_1 U^{**}\left(2 - \frac{U}{U^{**}} - \frac{U^{**}}{U}\right) + \alpha U^{**} V^{**}\left(1 - \frac{U^{**}}{U}\right) + \omega I^{**}\left(1 - \frac{V^{**}}{VI^{**}}I\right)$$

$$-\frac{I^{**}}{I}\left(\frac{I^{**}\omega UV}{U^{**} V^{**}}\right) + (\alpha U^{**} V^{**})\left(\frac{\omega I^{**}}{\alpha U^{**} V^{**}}\right) \quad (61)$$

$$\dot{F} = \mu_1 U^{**}\left(2 - \frac{U}{U^{**}} - \frac{U^{**}}{U}\right) + \alpha U^{**} V^{**}\left(1 - \frac{U^{**}}{U}\right) + \omega I^{**}\left(1 - \frac{V^{**}}{VI^{**}}I\right)$$

$$-\frac{I^{**}}{I}\left(\frac{I^{**}\omega UV}{U^{**} V^{**}}\right) + (\omega I^{**}) \quad (62)$$

$$\dot{F} = \mu_1 U^{**}\left(2 - \frac{U}{U^{**}} - \frac{U^{**}}{U}\right) + \alpha U^{**} V^{**}\left(1 - \frac{U^{**}}{U}\right) + \omega I^{**}\left(1 - \frac{V^{**}}{VI^{**}}I\right)$$

$$+\omega I^{**}\left(1 - \left(\frac{I^{**} UV}{U^{**} V^{**} I}\right) + \right. \quad (63)$$

$$\dot{F} = \mu_1 U^{**}\left(2 - \frac{U}{U^{**}} - \frac{U^{**}}{U}\right) + \omega I^{**}\left(2 - \frac{V^{**}}{VI^{**}}I - \frac{I^{**} UV}{U^{**} V^{**} I}\right) + \alpha U^{**} V^{**}\left(1 - \frac{U^{**}}{U}\right) \quad (64)$$

Finally, since the arithmetic mean exceeds the geometric mean, i. e

$$AM = \frac{x_1 + x_2 + x_3 + \cdots + x_n}{n} \geq \sqrt[n]{x_1 + x_2 + x_3 + \cdots + x_n} = GM \text{ [14]}$$

It is follows that,

$$\mu_1 U^{**}\left(2 - \frac{U}{U^{**}} - \frac{U^{**}}{U}\right) \leq 0$$

$$\omega I^{**}\left(2 - \frac{V^{**} I}{VI^{**}} - \frac{I^{**} UV}{U^{**} V^{**} I}\right) \leq 0$$

$$\alpha U^{**}V^{**}\left(1-\frac{U^{**}}{U}\right)\leq 0 \qquad (65)$$

Furthermore, since all the model parameters are non-negative, it follows that $\dot{F}\leq 0$ for $R_o>1$, thus $\dot{F}$ is a Lyapunov function for sub system of the model (1)- (5) and is globally asymptotically stable. Therefore, it follows by Lassalle's Invariance Principle [14] that,

$$\lim_{t\to\infty}U(t)=U^{**},\quad \lim_{t\to\infty}V(t)=V^{**}\quad \text{and}\quad \lim_{t\to\infty}I(t)=I^{**} \qquad (66)$$

Since $I(t)\to I^{**} as\ t\to\infty$, it follows from the equation (4) at steady state, that

$$(\ )\to 0 \qquad \to\infty \qquad (67)$$

The epidemiological implication of the Theorem 1, is that Ebola virus will be establish in the system (or Body) when >1 and the immune responses against the Ebola virus in the cell population move toward zero as the virus established in the body.

CONCLUSION

This paper shown the positivity of solutions of the model equations (1)-(5), which implies, that the solutions remain positive for all time, t and the model is epidemiologically meaningful and well pose. Equation (22) and (28) showed the existence of virus free and virus persistence equilibria points. Equation (41) computed the basic reproduction number of the system and Equations (65), (66) & (67) shown the global stability of virus persistence equilibrium state and found that the virus persistence equilibrium is globally asymptotical stable (GAS) when $_0>1$.

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